38 are also separately rejected under 35 U.S.C. § 103(a) as being obvious over Greyer et al. in view of Gregory et al. (U.S. Patent No. 5,262,179).

The invention of the present application provides an improved solid compressed dosage form (i.e. tablet) for oral administration to permit delivery of high therapeutic levels of ibuprofen (greater than equal to 35% by weight of the composition) to a patient. In particular, this is achieved by including 3 to 20% by weight of an alkali metal (bi)carbonate in the composition.

Unexpectedly, the inclusion of an alkali metal (bi)carbonate enhances the compressibility of the pharmaceutical composition comprising a compressible filler and a disintegrant. Conveniently, the composition of the present invention permits a reduction in the amount of compressible filler component that would normally be required to achieve satisfactory compressibility, thereby allowing an acceptably sized tablet to be produced. Moreover, the composition of the present invention may be compressed by applying compression forces of above 80 MPa (i.e., a suitable force employed by standard tabletting machines (see page 6, lines 29 to 30 and page 13, lines 18 to 26) to produce tablets for direct administration to a patient having improved crush strength (i.e., hardness so that they do not break up during further manufacturing steps) which also exhibit an acceptable relatively fast disintegration time to permit an on-set hastened action.

In contrast to the presently claimed invention, Geyer et al. (U.S. 5,380,555) provides a chewable composition of low hardness so that a therapeutically effective amount of a drug may be delivered to a patient without the need for swallowing a tablet (see col. 1, lines 61 to 65). Thus, Geyer solves a completely different technical problem

than the one solved by the invention of the present application which relates to hard, highly compressed dosage forms suitable for swallowing by a patient.

Although the general disclosure of Geyer indicates that the chewable composition may include a buffering agent as an optional ingredient, which buffering agent may be selected from the list of sodium bicarbonate, sodium phosphates, or corresponding calcium salts or the like (see col. 6, lines 16 to 18), it is evident that none of the specific examples include all of the claimed component parts of the composition of the presently claimed invention, particularly in the claimed amounts, as suggested by the Examiner. Moreover, the general disclosure of Geyer does not provide an indication of suitable compressive forces which may be applied to the composition; instead, specific compressive forces, which are substantially less than the 80 MPa now claimed, are applied to compositions of the specific examples which do not include all of the features of the presently claimed composition. Applicants believe that the maximum tabletting force disclosed of 10,000 psi as exemplified in Example 5 equates to 68.95 MPa.

In this respect, Example 1 does not include a disintegrant or a buffering agent which as stated above is an optional ingredient. Furthermore, it relates to a granulated composition, and it is therefore not compressed. Example 3 does not include a disintegrant and relates to a powdered composition, and it is therefore not compressed. Example 5 only includes 14% ibuprofen instead of at least 35% ibuprofen, does not include an optional buffering agent, and is subjected to a compression force of 10,000 psi (approximately 68 MPa) rather than 80 MPa. Example 9 only includes 10% ibuprofen instead of at least 35% ibuprofen, it does not include an optional buffering

agent, and it is subjected to a compression force of 5,000 psi (approximately 34 MPa) rather than 80 MPa.

Consequently, it is apparent that a skilled person in order to arrive at the invention of the present application either from the general or specific disclosure of Geyer, would firstly have had to take the nonobvious step of selecting more than one preferred variable (such as a specified amount of a preferred buffering agent), including these additional variables into the composition and then take the further nonobvious step of subjecting the resultant composition to a compression force of above 80 MPa. All this in view of the fact that nowhere does Geyer teach or suggest that the inclusion of an alkali metal (bi)carbonate would, let alone could, produce a resultant composition having enhanced crush strength and desirable disintegration properties when compressed above 80 MPa, particularly as Geyer merely mentions that sodium bicarbonate is one of a selection of optional buffering agents and Geyer actively teaches away from high compressive forces.

For example, considering Example 5, not only should the ibuprofen content be increased to at least 35% by wt, but the skilled person then would have had to have been motivated to include an optional buffering agent, then would have had to have been motivated to select sodium (bi)carbonate as the buffering agent from a general list of buffering agents, and finally they then would have had to have been motivated to subject the composition to an increased compressive force of above 80 MPa when it is clear from the general disclosure that chewable as opposed to highly compressed dosage forms are desired. Clearly, the above procedure represents a number of

specific selections which in itself, in the light of an unexpected result as is the case in the present application, represents patentable subject matter.

Similarly, taking preferred features from the specific examples of Geyer and combining them with the general disclosure (see col. 8) also represents a selection and is not proper. For example, a skilled person must first select an ibuprofen content of above 35% by weight in view of the fact that the most preferred range is 1 to 25% by weight (col. 8, line 4), then the skilled person must take the nonobvious step of including a buffering agent, then they must take the further nonobvious step of selecting sodium bicarbonate as the buffering agent from a general list of buffering agents, and finally they must have been motivated to apply a compressive force of 80 MPa to the composition when it is clear from the specific examples that it is not essential that a force is applied, and even when such a force is applied then it should be far less than 80 MPa.

Independent claims 16 and 26 also include the same distinguishing features of claim 1 and the above arguments apply thereto.

For at least the above reasons, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) are respectfully requested.

Applicants respectfully submit that this application is in condition for allowance and such action is earnestly solicited. If the Examiner believes that anything further is desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below to schedule a personal or telephone interview to discuss any remaining issues.

Please charge any fee deficiency or credit any overpayment to Counsel's Deposit Account 01-2300.

Respectfully submitted,

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Attachments: Marked-Up Amendments to Claims

MARKED-UP AMENDMENTS TO CLAIMS

1. (Amended) A solid non-effervescent compressed dosage form suitable for oral administration comprising a homogenous admixture of a racemic ibuprofen medicament present to an extent of 35% or more by weight of the dosage form and a carrier material comprising

i) a compressible filler component combined with a disintegrating component;

ii) 3-20% solid alkali metal carbonate or bicarbonate by weight of the dosage form;

wherein the dosage form has a crushing strength in the range 6.5-15 Kp and a disintegration time of less than 10 minutes <u>at a compression force above 80 MPa</u>,

provided that the ibuprofen medicament does not contain a calcium salt of ibuprofen in combination with an alkali metal salt of ibuprofen.

16. (Amended) A method of obtaining an onset-hastened analgesic and/or anti-pyretic response comprising the oral administration of a non-effervescent compressed solid dosage form comprising 35% or more by weight of a racemic ibuprofen medicament in homogeneous admixture with a carrier material comprising

i) a compressible filler component combined with a disintegrating component, and

ii) 3-20% solid alkali metal carbonate or bicarbonate by weight of the dosage form,

wherein the dosage form has a crushing strength in the range of 6.5-15 Kp and a disintegration time of less than 10 minutes at a compression force above 80 MPa,

provided that the ibuprofen medicament does not include a calcium salt of ibuprofen in combination with an alkali metal salt of ibuprofen.

26. (Amended) A solid formulation having a layer comprising a composition comprising a racemic ibuprofen medicament in homogeneous admixture with a carrier material, the racemic ibuprofen medicament being present to an extent of 35% or more by weight of the composition and the carrier material comprising a compressible filler component combined with a disintegrating component characterised in that the carrier material comprises 3-20% solid alkali metal carbonate or bicarbonate by weight of the dosage form,

wherein the composition is capable of compression to provide a layer having a crushing strength in the range of 6.5-15 Kp and a disintegration time of less than 10 minutes at a compression force above 80 MPa.